REMARKS

Claims 1-3 and 21-28 were pending in this application when last examined. Claims 1 and 26 are currently amended. Claims 27-28 have been canceled and new claims 30-33 have been added. The specification has also been amended to correct typographical errors, and to include sequence identifiers and a sequence listing.

Support for the amendments and the new claims can be found in the specification and original claims as filed. Support for amended claims 1 and 26 and new claims 30-33 can be found, for example, in the specification at pages 30-31 and in Examples 1-11. No new matter has been added.

INVENTORSHIP

Applicants duly note the comments provided in the Office Action regarding inventorship.

As explained in the August 25, 2009 Response, the International Bureau deleted inventor Paul COHEN on January 28, 2005 and deleted inventor Gabriel PELTRE on April 11, 2005, as are reflected by two Form PCT/IB/306 documents. These documents are already of record, but additional copies are included as an attachment for the convenience of the Examiner. At the time that this application entered the National Stage, the inventorship of the instant application was established as Daniel ZAGURY and Helene LE BUANNEC only. Thus, the only requirement necessary in

regard to addressing this issue is a new oath or declaration as indicated under 37 CFR 371(c)(4)(f).

Accordingly, Applicants submit herewith a new Declaration duly executed by the two inventors of the instant application.

AMENDMENTS TO THE SPECIFICATION

Applicants amend the specification to address issues regarding compliance with the sequence rules. The amended specification includes sequence identifiers at pages 38 and 63 (SEQ ID NO. 1-2). Applicants also submit a sequence listing to place the application in compliance with the Sequence Rules under 37 C.F.R. § 1.821-1.825.

Enclosed is a Sequence Listing in both paper and computer readable form (CRF) as required by 37 C.F.R. § 1.821(c) and (e). The specification has been amended to insert the attached paper copy and CRF of the Sequence Listing. Support for such can be found in the originally filed application. No new matter has been added. Accordingly, the submission complies with 37 C.F.R. § 1.821(g). The content of the paper and computer readable copies of the Sequence Listing are the same, and thus this submission complies with 37 C.F.R. § 1.821(c) and (e).

The amended specification also corrects obvious typographical errors in Example 9 and in Example 32.

CLAIM REJECTION - 35 U.S.C. § 102

At page 2, item 7, the Office Action maintains the rejection of claims 1-3 and 21-25 under 35 U.S.C. § 102(b) as being anticipated by ZAGURY et al. (WO 02/011759 A1; US 2004/0028647). Applicants respectfully traverse the rejection.

At page 5, the Office Action offers helpful suggestions regarding the addition of "product-by-process" claim limitations to the instant claims in order to further distinguish over ZAGURY. Currently amended claim 1 is directed to a stable immunogenic product for inducing antibodies raised against a TNFα protein. The product comprises immunogenic heterocomplexes comprising TNFα protein molecules associated with KLH carrier protein molecules, more than 1% and less than 40% of the TNFα protein molecules are directly covalently linked to the KLH carrier protein molecules, and more than 60% of the TNFα protein molecules are non-covalently associated with the KLH carrier protein. Finally, the stable immunogenic product is produced by a process comprising a specific series of steps that includes incubating TNFα proteins and KLH carrier molecules in a molar ratio TNFα:KLH ranging from 10:1 to 50:1 in the presence of glutaraldehyde. ZAGURY fails to teach or suggest such a product.

In addition to the reasons for distinguishing over ZAGURY provided in the previous responses filed with the Office, amended claim 1 now recites specific product by process limitations. In particular, the process features incubating a

TNFα:KLH molar ratio ranging from 10:1 to 50:1 in the presence of glutaraldehyde, stabilizing with formaldehyde, and blocking with glycine. The process steps featured in claim 1 affect the physical properties of the immunogenic product such that more than 1% and less than 40% of the TNFα protein molecules are directly covalently linked to the KLH carrier protein molecules, and more than 60% of the TNFα protein molecules are non-covalently associated with the KLH carrier protein. ZAGURY fails to teach or suggest a product having the features, and produced by the process, as presently claimed.

As detailed in the previous Amendment, the immunogenic compositions disclosed in ZAGURY comprise heterocomplexes of biological factor and KLH, wherein essentially 100 percent of the biological factor is covalently linked to the KLH carrier protein molecules. The ZAGURY preparation provides an immunogenic composition wherein virtually 100% of the biological factor is covalently bound to the KLH carrier protein, but with zero biological factor molecules that are non-covalently associated with the KLH carrier protein.

In contrast to ZAGURY, the presently claimed immunogenic product comprises heterocomplexes of TNFα protein molecules associated with KLH carrier protein molecules, wherein less than 40% of the TNFα molecules are directly covalently linked to the KLH carrier protein molecules, and more than 60% of

the TNFα protein molecules are non-covalently associated with the KLH carrier protein. This distinguishes over ZAGURY.

For all of these reasons, ZAGURY fails to teach or suggest, and fails to anticipate claims 1-3 and 21-25. Accordingly, Applicants request reconsideration and withdrawal of the rejection.

NEW CLAIMS 30-33

New claims 30-33 depend from claim 1 and include additional process steps that further distinguish the claimed immunogenic product over ZAGURY.

PROVISIONAL OBVIOUS-TYPE DOUBLE PATENTING REJECTION

At page 6, item 8, the Office Action maintains a provisional nonstatutory double patenting rejection of claims 1-3 and 21-25 over claim 1 of co-pending Application No. 11/735319. Applicants respectfully traverse the rejection.

Present claim 1 is directed to a product comprising protein immunogenic heterocomplexes consisting of associations between TNFα protein and KLH carrier protein and produced by a specified process. Claims 2-3 and 21-25 depend from claim 1.

In contrast to the instant claims, claim 1 of the '319 application is directed to a composition comprising inactivated TNFα or peptides of TNFα, wherein the TNFα has been inactivated by subjecting the TNFα to chemical treatment. The claims of the

‘319 application, however, fail to teach or suggest an immunogenic product comprising protein heterocomplexes between TNFα protein and KLH carrier protein, and/or covalent linkages to the KLH carrier protein. In the ‘319 application, chemical treatment is used to inactivate TNFα but does not require heterocomplex formation.

The presently claimed heterocomplexes are produced by a series of steps that includes a specific molar ratio of TNFα and KLH, along with a series of glutaraldehyde, formaldehyde and glutamine treatment steps. Claim 1 of the ‘319 application fails to teach or suggest producing heterocomplexes by such a specific process.

For example, the ‘319 product as recited in claim 1 is produced by a method where TNFα/peptide is first inactivated with formaldehyde and then treated with glutaraldehyde. In distinction, the presently claimed product is prepared by a method where TNFα protein, non pre-activated KLH carrier and glutaraldehyde are all incubated together. This is then followed by a formaldehyde step and further a glutamine step.

For at least these reasons, claim 1 of the ‘319 application does not teach or suggest, and would not have rendered obvious, present claims 1-3 and 21-25. Accordingly, Applicants request reconsideration and withdrawal of the rejection.

CONCLUSION

Entry of the above amendments is earnestly solicited. Applicant respectfully requests that a timely Notice of Allowance be issued in this case.

Should there be any matters that need to be resolved in the present application, the Examiner is respectfully requested to contact the undersigned at the telephone number listed below.

The Commissioner is hereby authorized in this, concurrent, and future submissions, to charge any deficiency or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

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HJV/fb

APPENDIX:

The Appendix includes the following items:

☒ - Sequence Listing in paper and computer readable form

☒ - Signed Declaration by Inventors

☒ - Form PCT/IB/306 - PELTRE

☒ - Form PCT/IB/306 - COHEN